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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/537,394

06/02/2005

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INN-123

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EXAMINER

SZNAIDMAN, MARCOS L

ART UNIT

PAPER NUMBER

1611

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/537,394	<b>Applicant(s)</b> ROMAGNE ET AL.	
	<b>Examiner</b> MARCOS SZNAIDMAN	<b>Art Unit</b> 1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 19 February 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 80-103 is/are pending in the application.
- 4a) Of the above claim(s) 89,96-99 and 103 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 80-88,90-95 and 100-102 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>See Continuation Sheet</u> .                                  | 6) <input type="checkbox"/> Other: _____                          |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :8 pages / 06/29/2007 and 09/14/2007.

## DETAILED ACTION

This office action is in response to applicant's reply filed on February 19, 2008.

### ***Election/Restrictions***

Applicant's election of Group I (claims 80-98 and 100-103) and the following species: 3-(bromomethyl)-3-butanol-1-yl-diphosphate (BrHPP or Phosphostim) as the compound of Formula II, and renal carcinoma as the solid tumor, in the reply filed on February 19, 2008, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

### ***Status of Claims***

Claims 80-103 are currently pending and are the subject of this office action.

Claims 89, 96-99 and 103 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions/species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on February 19, 2008.

Claims 80-88, 90-95 and 100-102 are presently under examination.

***Priority***

The present application is a 371 of PCT/IB03/06375 filed on 10/02/2003, and claims priority to EPO 02292963.2 filed on 12/02/2002.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

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were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 80-88, 90-95 and 102 are rejected under 35 U.S.C. 103(a) as being unpatentable over BioNews ([http://www.investinbiotech.com/pressroom\\_release.php?id+644](http://www.investinbiotech.com/pressroom_release.php?id+644), July 8, 2002) as evidenced by Espinosa et. al. (Journal of Biological Chemistry (2001) 276:18337-18344).

Claims , 80-81, 86-88, 90-93 and 102 recite a method of treating a solid tumor (species elected: renal carcinoma), comprising the administration of a composition gamma-delta cell activator (species elected: Phosphostim).

For claims, 80-81, 86-88, 90-93 and 102, BioNews teaches a method of treating renal carcinoma with Phosphostim, an activator of T gamma-delta cells.

The statements in claims 80: "in an amount sufficient to induce at least 5-fold increase in the gamma-delta T cell population", claim 81: "wherein said gamma-delta T cell activator is provided in an amount sufficient to induce at least 10-fold increase in the gamma-delta T cell population in a subject", claim 86: "wherein said gamma-delta T cell activator is provided in an amount sufficient to expand the gamma-delta T cell population in a subject to reach between 30-90% of total circulating lymphocytes in a subject", claim 87: "wherein the biological activity of gamma-delta T cells is increased in

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said subject”, claim 90: “wherein the gamma-delta T cell activator is a composition comprising a compound capable of inducing the proliferation of a gamma-delta T cell in a pure population of gamma-delta T cell clones when said compound is present in culture at a concentration of less than 1 mM”, are inherent properties of the method developed described in BioNews (i.e. it was already present in the prior art, even though the prior art does not recognize that property) as evidenced by Espinosa et. al. Espinosa et. al. teach that BrHpp (species elected) increases the gamma-delta T cell population among total T cells in culture up to 20% at 12.5 nanomolar, 30% at 25 nanomolar and 50% at 100 nanomolar (see page 18340, Figure 4 B)

At the time of the invention, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine the teachings BioNews (treating renal cancer with Phosphostim), with the motivation of treating renal cancer, thus resulting in the practice of claims 80-81, 86-88, 90-93 and 102 with a reasonable expectation of success.

Claims 82-85 and 94-95 recite the same limitations as claim 80, further comprising different dosage regimes for the treatment of renal cancer with Phosphostim. It is within the capability of the ordinary artisan to determine these amounts for a particular patient and adjust dosage amounts based on the observed clinical effectiveness.

Why are you examining an invention involving interleukins? This is not our art.

Claims 100-101 are rejected under 35 U.S.C. 103(a) as being unpatentable over BioNews ([http://www.investinbiotech.com/pressroom\\_release.php?id+644](http://www.investinbiotech.com/pressroom_release.php?id+644), July 8, 2002)

as evidenced by Espinosa et. al. (Journal of Biological Chemistry (2001) 276:18337-18344) as applied to claims 80-88, 90-95 and 102 above, and further in view of Negrier et. al. (The New England Journal of Medicine, (1998) 338:1272-1278).

Claim 100 recites the same limitations as claim 80, further comprising separately administering to a subject in need thereof an effective amount of a gamma-delta T activator and an interleukin-2 polypeptide.

BioNews teaches all the limitations of claim 100, except for the administration of an interleukin-2 polypeptide. However, Negrier et. al. teach that Interleukin-2 induce notable tumor regression in a limited number of patients with metastatic renal-cell carcinoma (see title and abstract).

Claim 101 recites the same limitations as claim 100, wherein the interleukin-2 polypeptide is administered over a period of time between 1 and 10 days. For claim 101, Negrier further teaches that interleukin-2 was administered as a five-day continuous intravenous infusion (see page 1273, under treatment, second paragraph).

At the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to treat renal cancer combining two compositions (Phosphostim and Interleukin-2) each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art (see MPEP 2144.06). *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) claims to a process preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be *prima facie*



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obvious. All this would result in the practice of claims 100 and 101 with a reasonable expectation of success.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward can be reached on 571 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MLS  
April 15, 2008

/MP WOODWARD/  
Supervisory Patent Examiner, Art Unit 1615